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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,619	01/13/2006	Amram Mor	31019	9196

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,619	MOR, AMRAM	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species of SEQ ID NO:1 in the reply filed on 5/21/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-23 read on the elected species and are under consideration.

Specification

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (for example page 4 line 10, page 21 line 5). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of trademarks, (for example page 9 line 24 - DACRON, page 10 line 6, page 23 line 16-18, page 31 lines 1,2,29) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.
>
> Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, briefly, the claims are drawn to a medical device/implant comprising 'a peptide having at least 9 amino acid residues and less than 51 amino acid residues' including a particular sequence. The claims are also drawn to methods of fabricating/using the medical implant in which the surface of the implant is capable of killing or preventing the growth of a pathogen. It is noted that the specification broadly defines peptide (page 16) to include analogs and peptidomimetics.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high regarding anti-microbials in general, however, the knowledge in the art is low with regard to understanding which amino acid sequences will have a particular function given that substitutions cannot be predicted a priori.

(2) Partial structure:

Examples given in the specification include the examples of Table 1 in which peptides of 9-14 amino acids are shown. The claims are drawn to peptides of up to 50 amino acids, however the specification does not provide a sufficient number of examples of such peptides to describe the entire genus. Further, the specification (page 16) defines peptides to include analogs and

peptidomimetics. However, specific examples of analogs or peptidomimetics are not provided. There are hundreds of possible polypeptides that fall within the scope of the claims. Since there are a substantial variety of polypeptides possible within the genus, the limited examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see *Gostelli* above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The polypeptides are described as being capable of killing or preventing the growth of a pathogen. However, there is no disclosed correlation between this functional characteristic and any structure. One of skill in the art would not recognize which peptides, analogs, and peptidomimetics would prevent the growth of a pathogen and one could not a priori predict the properties.

(5) Method of making the claimed invention:

The specification (page 15) provides guidance on making peptides in general which is well known in the art, however given the unpredictable nature of amino acid substitution one would not know which peptides/analogs/peptidomimetics to make.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,8,17 is/are broad and generic, with respect to all possible peptides encompassed by the claims. The possible structural variations are limitless to any peptides, analogs, or peptidomimetics. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the polypeptides beyond those polypeptides specifically disclosed in the examples in the

specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of polypeptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of polypeptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 8-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the fabrication and use of devices/grafts with particular peptides (such as the peptides described in example 1), does not reasonably provide enablement for the fabrication and use of devices/implants with any peptide/analog/peptidomimetic as claimed having the property of being able to kill or prevent the growth of any microbial pathogen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d

731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are also drawn to methods of fabricating/using the medical implant in which the surface of the implant is capable of killing or preventing the growth of a pathogen. It is noted that the specification broadly defines peptide (page 16) to include analogs and peptidomimetics.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The claims are drawn to a medical device or implant capable of killing or preventing the growth of a pathogen in which a peptide/analog/peptidomimetic is used. However, the knowledge in the art is low with regard to understanding which amino acid sequences will have a particular function given that substitutions cannot be predicted a priori. With regards to the effect of amino acid substitution in a peptide or protein, the art is unpredictable.

MATHISON (US Patent 6,586,403 B1) teaches that "Restriction on the amino acid substitutions that are tolerated in analogues of FEG/feG are described [...] although a theory for the rational substitution of amino acids in to the peptides that permits the prediction of biological activity of specific peptides is not apparent. For example, it is not obvious which aromatic or

aliphatic substitutions in position 1 of tri- or dipeptides would possess biological activity in the four assays examined" (column 12, lines 22-30).

Further, MPEP § 2144.08 states, "The effect of a conservative substitution on protein function depends on the nature of the substitution and its location in the chain. Although at some locations a conservative substitution may be benign, in some proteins only one amino acid is allowed at a given position. For example, the gain or loss of even one methyl group can destabilize the structure if close packing is required in the interior domains. James Darnell *et al.*, *Molecular Cell Biology* 51 (2d ed. 1990)."

(5) The relative skill of those in the art:

The level of skill in the art is high regarding anti-microbials in general, however, the knowledge in the art is low with regard to understanding which amino acid sequences will have a particular function given that substitutions cannot be predicted a priori.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

An example (example 1) is provided in which peptides are tested for anti-microbial functionality. However, the specification does not provide examples for the breadth of the peptides/analogs/peptidomimetics possible. Further, examples of making specific analogs/peptidomimetics with anti-microbial properties have not been provided. Specifically, one of skill in the art would not accept that all peptides/analogs/peptidomimetics described would function as anti-microbials.

(8) The quantity of experimentation necessary:

Experimentation is required in numerous areas particularly related to how to make specific peptides/analogs/peptidomimetics with anti-microbial properties and determination if it would be a useful composition against any microbial pathogen. Considering the state of the art as discussed by the references above, particularly with regards to the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2,4-5,8,14-17,19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Mor (WO 01/10887 as cited in IDS).

Briefly, the claims are drawn to a medical device or implant comprising a body including a particular peptide; methods of fabricating the medical device or implant; methods of using the medical implant. It is noted that the term 'body' used in the claims has been broadly interpreted to include the common definition of 'a mass of matter distinct from other masses'.

Mor teaches the peptide ALWKTLLKKVLKA (claim 1 of WO 01/10887) which is the elected peptide of the current invention. Mor teaches (claim 15) that the peptide can be attached to the membrane of a red blood cell (i.e. a body). The surface of the red blood cells are composed of polypeptides. Mor further teaches that the complex can be implanted into the body (for example, claim 31). Mor teaches that the peptide can be amidated (claim 1). Mor teach a method of attaching/fabricating (claim 52) the peptide to the red blood cell. Mor teaches a method of prevention/admisinstration (claim 57) in which the implant is introduced into the subject.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mor (WO 01/10887 as cited in IDS) and further in view of Krieger et al. (US 2003/0232750). It is noted that the priority date of Krieger is Oct. 18, 2002 bases on flowchart III of MPEP 706.02(f)(1).

Briefly, the claims are drawn to a medical device or implant comprising a body including a particular peptide; methods of fabricating the medical device or implant; methods of using the medical implant. It is noted that the term 'body' used in the claims has been broadly interpreted to include the common definition of 'a mass of matter distinct from other masses'.

The teachings of Mor are above. Briefly, Mor teaches specific compositions and methods of the current invention. Mor does not expressly teach peptide surface densities, solution concentrations, peptide exposure times, or the use of rifampin as an antibiotic.

It would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. peptide surface densities, solution concentrations, peptide exposure times), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

Krieger teach peptide compositions and methods for treating infections (abstract). Krieger specifically teach the dermaseptin peptides (Table 1). Krieger teach that a medical device is coated with the peptide analogs and may further comprise an antibiotic (section 0020). The methods of treatment use a combination of cationic peptides and antibiotic agents (section 0025). Krieger specifically teach rifampin as an antibiotic agent (Table 8). Kreiger teach that the medical devices can be used as grafts (section 0217) and that the peptides and antibiotics can be coated onto the medical device (section 0218).

Since both Krieger and Mor teach the use of dermaseptins for antimicrobial activity, one would have been motivated to use a specific embodiment of Krieger in which rifampin is added along with the peptide. All of the components are present in the two references. It would have been obvious to one of skill in the art to use the known products in the art in the same way for improved anti-biotic activity in a predictable manner.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rtn

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